

A METHOD OF INDUCING OR ENHANCING CHONDROGENESIS WITH
EXTRACELLULAR MATRIX CONTAINING BMP-4

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4/05 5 This application claims priority from Provisional application Serial No
Background of the Invention 601,97,235 filed 4/14/2000

5 The limited capacity of articular cartilage to
regenerate represents a major obstacle in the management of
degenerative and traumatic joint injuries. The maintenance
of a functional joint surface requires that articular
10 chondrocytes respond to extracellular signals that are
generated from growth and differentiation factors,
mechanical stimuli, and interactions with specific
components of the extracellular matrix. The invention is
directed to an extracellular matrix of type I collagen, type
15 II collagen, type I collagen plus hyaluronate, or type II
collagen plus hyaluronate, and bone morphogenetic protein-4
(BMP-4). A combination of BMP-4 with differentiation factor-
5 (GDF-5) is also useful.

20 Coordinated function of many cell types is regulated
by integration of extracellular signal derived from soluble
factors inducing growth factors and insoluble molecules such
as extracellular matrix (ECM). The skeletal elements of the
vertebrate limb are derived during embryonic development
from mesenchymal cells, which condense and initiate a
25 differentiation program that result in cartilage and bone.
Bone morphogenetic proteins may play a crucial role in
mesenchymal condensations in skeletal patterning, including
the process of joint formation.

30 Despite the importance of joint formation in
skeletal patterning and human disease, relatively little is
known about the molecular mechanisms that control where and
when a joint will form. In the limb, joints typically arise